Contains Nonbinding Recommendations

Draft Guidance on Esomeprazole Magnesium

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Esomeprazole Magnesium

Form/Route: Delayed Release Capsule/Oral

Recommended studies: 3 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 40 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments: Applicants may consider using a reference-scaled average bioequivalence approach for esomeprazole. If using this approach, please provide evidence of high variability in the bioequivalence parameters of AUC and/or C_{max} (i.e., within-subject variability $\geq$ 30%). Please refer to the Progesterone Capsule Draft Guidance for additional information regarding highly variable drugs.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 40 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional Comments: Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed studies.

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3. Type of study: Sprinkle
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 40 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional Comments: Fasting study, with contents sprinkled over a spoonful of applesauce in accordance with the approved labeling of the RLD.

Analytes to measure: Esomeprazole using an achiral assay.

Bioequivalence based on (90% CI): Esomeprazole

Waiver request of in-vivo testing: 20 mg based on (i) acceptable bioequivalence studies on the 40 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in-vivo testing.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. For dissolution method development, please refer to USP, "Delayed-Release (Enteric-Coated) Articles-General Drug Release Standard."

Esomeprazole is an acid labile drug substance; therefore, please measure esomeprazole from the beadlets of the EC capsule and not from the dissolution medium (0.1N HCl) during the acid stage. Using 12 additional capsules of the test and reference products, proceed to the buffer stage. Dissolution specifications will be determined upon review of the data in the ANDA.